

# Cardiovascular Risk Factors. A Multicenter Uncontrolled Follow-Up Study

JUDITH M. ZILBERMAN, LUIS CICCIO, ELIANA WORONKO, NORA VAINSTEIN, VANINA SCZCYGIEL, ROGER GHIGI, SANDRA GRIPPO, ALBERTO S. VILLAMIL<sup>MTSAC</sup>, ON BEHALF OF THE ENASE GROUP

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## Address for reprints:

Dra. Judith M. Zilberman  
Av. Las Heras 2910 - 1.º Piso "A"  
(C1425AST) CABA  
Phone number: +54911 50045420  
e-mail: juzilberman@gmail.com

## SUMMARY

### Background

Cardiovascular disease is still one of the leading causes of mortality in our country. It has been well documented that adequate changes in lifestyle are beneficial for primary and secondary prevention. However, it is difficult to apply or maintain these measures in the real world. The ENASE study was developed as a program to train physicians in the knowledge of good dietary habits and exercise to help patients to incorporate healthy behaviors in everyday life.

### Objective

To evaluate if a plan designed to train attending physicians can produce changes in the patients.

### Material and Methods

We conducted a prospective, multicenter and uncontrolled study on 508 patients with a follow-up of three years in 17 provinces and in the Autonomous City of Buenos Aires.

Statistical analysis was performed using the paired Student's t test and the Wilcoxon test.

### Results

With the help of primary physicians, this population increased physical activity and made significant changes in eating habits. Blood pressure, triglycerides, LDL-cholesterol and blood sugar levels decreased significantly and progressively from the first to the third year of follow-up. HDL-cholesterol increased significantly while body weight showed a slight and non-significant reduction.

The prescription of medical treatment did not change during the three years, except for a greater use of statins in accordance with the recommendations suggested by national guidelines.

### Conclusions

This study demonstrates that a plan focused on educating and training physicians produces significant benefits on the cardiovascular health of patients.

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**Key words >** Education - Prevention - Cardiovascular Risk Factors - Exercise - Nutrition

## Abbreviations >

<b>CAT 1</b>	Angiotensin II Type 1	<b>ENASE</b>	Encuesta NAcional de SEguimiento sobre factores de riesgo cardiovascular (Cardiovascular risk factors follow-up national survey)
<b>HDL-C</b>	High density lipoprotein-cholesterol	<b>AST</b>	Aspartate aminotransferase
<b>LDL-C</b>	Low density lipoprotein-cholesterol	<b>ALT</b>	Alanine aminotransferase
<b>WHO</b>	World Health Organization		
<b>DBP</b>	Diastolic blood pressure		
<b>SBP</b>	Systolic blood pressure		

## BACKGROUND

Cardiovascular diseases are responsible for 30% of all deaths worldwide, above the number of deaths due to infections, maternal and perinatal conditions, and nutritional deficiencies combined. (1) Forty-six percent of deaths occur in persons < 70 years. (2)

Cardiovascular prevention is an important individual and social tool that may reduce the incidence of death and disability. Its early implementation as well as patients adherence are essential to achieve these goals. Changes in lifestyle and drug therapy are the two strategies used for prevention and both have proved to be useful.

Controlled studies have demonstrated that lifestyle changes reduce the risk of developing cardiovascular diseases in the mid- and long-term. In Canada, 290 deaths per 100,000 patient-years were prevented in high cardiovascular risk patients over 10 years of follow-up. (3, 4)

The international guidelines address the importance of cardiovascular risk factors control (5-10) by losing body weight for those with overweight, performing physical activity, smoking cessation, moderation of alcohol intake, increased fresh fruit and vegetables and reduced saturated fat intake, reduction of dietary sodium and increased potassium intake.

The efficacy of these measures is counterbalanced by the difficulty in achieving long-term patient adherence. For this reason, many patients who could benefit from adopting lifestyle changes require drugs to reduce high blood pressure values, blood sugar and plasma lipid levels.

Studies evaluating long-term benefits of lifestyle changes differ in terms of duration and of results obtained. In general, those studies lasting less than two year did not show clear benefits in the reduction of cardiovascular events. A meta-analysis, which included 30,902 patients from 27 studies showed a reduction in the incidence of combined cardiovascular events by 16% while reductions of up to 24% were seen in trials with longer follow-up. (11)

These data support the hypothesis that the implementation of program based on training physicians might achieve better patient's adherence to lifestyle changes programs in Argentina with better outcomes in cardiovascular health in the mid- and long-term.

The study evaluated:

1. The prevalence of cardiovascular risk factors in an outpatient population in Argentina.
2. The feasibility of training physicians in hygienic and dietetic measures and the impact in the study population.
3. Lifestyle changes achieved through dietary counseling and indication of regular physical activity in patients consulting general practitioners, internists and cardiologists over three years.

In addition, the study evaluated the necessary

time to achieve significant changes in cardiovascular risk factors by using a lifestyle modification program.

## MATERIAL AND METHODS

We conducted a prospective, multicenter, three-year follow-up study (from March 2003 to December 2007).

The study was designed and conducted by the Fundación para el Estudio de la Hipertensión Arterial y la Prevención de los Factores de Riesgo Cardiovascular (FUNDAPRES, Study of Hypertension and Prevention of Cardiovascular Risk Factors Foundation). The patients included were treated at different institutions. No changes on drug therapy were made except for those decided by the attending physician. Treatment was based on the current recommendations provided by each scientific society for each individual case.

### Inclusion criteria

- Patients > 21 years of both genders, with or without present illness and with or without medical treatment at the first visit, who could complete a three-year follow-up.

### Exclusion criteria

- Patients < 21 years or those unable to make regular medical visits.
- Pregnancy or lactation.
- Patients with end-stage conditions or whose life expectancy was < 2 years.
- Patients with severe kidney failure (glomerular filtration rate < 30 ml/min) or liver disease (AST and/or ALT three times the upper limit of normal values).
- History of cognitive deficit, Alzheimer's disease or dementia.
- Patients unable or with contraindications to exercise.
- Drug abuse.
- Patients without a permanent home address or who are unable to continue regular follow-up visits due to other diseases.

The study protocol was approved by the FUNDAPRES institutional committee. Each principal investigator was considered as the trial site and was assigned an identification number. The information of the subjects included in the study was completed anonymously.

### Survey form

Data for further analysis were collected using an electronic form. The targets of the ENASE study (Encuesta Nacional de Seguimiento sobre factores de riesgo cardiovascular, Cardiovascular risk factors follow-up national survey), were entered on the website [enase.fundapres.org.ar](http://enase.fundapres.org.ar), together with the instructions, scientific information (relevant guidelines and publications) and supporting material to carry out patient's lifestyle changes (physical activity and healthy diet according to patient's disease).

The initial education program included the discussion of communication strategies, material related with nutrition (different diets), counseling about how to start physical activity to achieve an adequate training intensity. Written and graphic material were provided.

Then the investigation team met once a year to plan strategies, improve the quality of the information recorded and provide continuing education program to the investigators in subjects related to cardiovascular prevention, lifestyle changes and current topics. Also, the program included a practical demonstration of the physical exercises recommended.

The following data were recorded at each visit over the

study period:

- Personal history, gender, age, history of hypertension, diabetes and/or dyslipemia, family history of the same conditions, and target-organ damage (retina, kidney or cardiovascular system).
- Drug therapy taken at visit 1 by generic name and daily dose (mg/day).
- Laboratory tests: blood sugar levels, total cholesterol, HDL-C, LDL-C and triglycerides within the last month or at visit 1.
- Oral glucose tolerance test was recommended in patients with impaired fasting glucose (values between 111 and 125 mg/dl). A blood sample was taken to measure plasma glucose level before and 120 min after the administration of 75 mg of glucose anhydrous.
- Blood pressure was measured following the recommendations of the American Heart Association and the Latin American Consensus Statement on Hypertension. (8, 12, 13)
- Weight (kg) (14, 15), height (m) (14, 16) and waist circumference (cm) were measured as recommended by the international guidelines. (14, 15)
- Patients were asked if they performed regular exercise (type, weekly frequency, duration of each session and whether they continued or had given up).
- The dietary survey recorded the type of nutrient intakes and frequency of consumption by day, week or month. Consumption of red and white meat, cold cuts, diary, cheese, fruit and vegetables, legumes, candies and jam, pasta, dried fruit, eggs and bread was recorded.
- Patients were asked about alcohol intake (wine, beer, distilled spirits), age of drinking onset and amount by day, week or month.
- Smoking habits, history of smoking and current smoking, type of tobacco (cigarette, cigar, pipe), age of smoking onset and for those who gave up smoking, time since smoking cessation.
- Work activity
- Education level

Five visits took place during the study: visit 1 or initial visit (V1), visit 2 (V2) at 6 months, visit 3 (V3) at 1 year, visit 4 (V4) at 2 years and visit 5 (V5) at 2 years. The information mentioned in the electronic form was recorded in each visit.

### Dietary information

Before the study started, the investigators were trained in several nutrition-related aspects. Models of dietary plans were designed to suit the needs of each patient. The investigators received written instructions with guidelines to achieve patients' adherence, which included four general items:

1. To change the concept of diet for eating plan.
2. To explain the enhancing effect of the triad: medication + eating plan + physical activity.
3. To avoid strict nutrition indications, offering the best choices, if possible, to improve the adherence to lifestyle changes.
4. To send the message: "something can be always implemented".

Four models of basic eating plans were designed: low sodium plan, low-calorie plan (with the option of low sodium variant), diabetes plan (with the option of low sodium variant) and low-fat plan (with the option of low sodium variant).

The investigators received brochures with white meat, sauces and no-salt seasoning recipes and special diet plans

specific for different conditions (digestive or renal diseases). (14, 15, 17)

### Information about physical activity

The investigators were trained on physical activity counseling. Written instructions were developed for the patients, encouraging them to start physical activity in sedentary patients. The patients were advised to engage in long-lasting physical activities rather than intense exercise training. Initially, exercise should not last longer than 15 to 20 min, increasing after one or two weeks according to patients' tolerance. All the patients were asked to rate their perceived exertion using the modified Borg scale which monitors the intensity of effort ranging from 0 (nothing at all) to 10 (maximal effort), and were advised to keep a rating between 1 (very weak effort) and 4 (somewhat strong effort). Finally, patients were advised to consult their physicians in case warning signs developed.

Each patient received an elastic band and an illustrative brochure with aerobic exercises and strength endurance training as a complement to physical training in patients who were able to make them. The goal of these exercises was to improve muscle oxidative metabolism and to reduce body fat. These exercises could be done in any place, even at the patient's home. (19)

The prevalence of cardiovascular risk factors in this outpatient population was analysed in the initial visit: hypertension, type 2 diabetes mellitus, impaired glucose tolerance, dyslipemia, smoking habits, alcoholism, sedentary life, obesity or overweight, and associated clinical conditions):

The performance of physical activity and its impact on variables as body weight, waist circumference and functional capacity were evaluated.

The physical activity energy for a subject 1.70 m tall who weighed 70 kg was calculated by multiplying the frequency and the duration of each type of activity reported by its expenditure in kcal/min (20) (Table 1).

### Statistical Analysis

Sample size calculation: the intervention was conducted in all the patients as lifestyle changes recommendations apply to all patients with cardiovascular risk factors. The sample size was calculated following the WHO STEPwise approach to Surveillance (21), and was estimated in 480 subjects with a 1:1 male-female ratio, considering a 20% loss to follow-up.

Quantitative variables were analyzed according to their distribution and were expressed as averages and standard deviations or medians and interquartile ranges. Percentage or proportions were used as summary measures of quantitative variables. McNemar's test or Cochran's test

**Table 1.** Quantification of physical activity

Physical activity	kcal/min
Gym	125
Walking	160
Biking	300
Lift weights	250
Golf	168
Sports	201

The physical activity energy for a subject 1.70 m tall who weighed 70 kg was calculated by multiplying the frequency and the duration of each type of activity reported by its expenditure in kcal/min

were used for testing the null hypothesis of inexistence of changes between two correlated proportions or greater. The paired Student's t test and the Wilcoxon test were used to compare continuous variables of any visit with the initial visit. ANOVA and the non-parametric repeated measures Friedman test were used to compare three visits or greater. An error  $\alpha < 0.05$  was considered statistically significant and Bonferroni test was used for multiple comparisons.

## RESULTS

At the initial visit, the following prevalences were recorded: hypertension 78%, dyslipemia 60%, diabetes mellitus 17.51%, central obesity 43.3% and smoking habits 13%. Table 2 shows the general and baseline characteristics of the population. Almost 50% of the population ate food that was not recommended or in larger amounts (32.5% consumed red meat more than

three times a week, 68.1% ate cold cuts, 42.7% candies and 49.8% jam).

Table 3 and Figures 1 and 2 show the behavior of the different risk factors and anthropometric measurements between the baseline visit (V1) and the final visit (V5). The greatest benefit was seen in patients with hypertension or dyslipemia at the initial visit compared with those who did not present these conditions.

In this population, drug therapy remained stable except for the greatest prescription of statins throughout the study. This was due to the increasing number of indications according to the international guidelines developed by the scientific societies while the study was being conducted (Figure 3) (333 patients in V1 and 457 in V5).

Patients who were not receiving statins also showed favorable outcomes in lipid plasma levels following non-pharmacological measures. LDL-C and triglycerides showed a significant reduction ( $p = 0.003$  and  $0.049$ , respectively) while HDL-C increased significantly ( $p = 0.006$ ).

The prevalence of smoking habits was reduced by 4% after the first year of the study.

The benefits of lifestyle changes were noticed from V2 (six months), when SBP, DBP, total cholesterol, LDL-C and triglycerides showed significant reduction. HDL-C increased significantly after the first year ( $p = 0.049$ ) (Figure 1).

## DISCUSSION

Cardiovascular disease is still the leading cause of death in our country despite the important progress in drug therapy (diuretics, beta blockers, calcium antagonists, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, aspirin, clopidogrel and statins, among others): The benefits of lifestyle changes are well-known and the information about how physical

**Table 2.** General and baseline characteristics of the population

Variable	n (%)
Gender	Women: 224 (44%) Men: 284 (56 %)
Waist circumference	Women: 106 (47%) Men: 114 (40%)
Diabetes mellitus	89 (17.51%)
Dyslipemia	306 (60%)
Hypertension	397 (78%)
Education level	Primary: 197 (38.78%) Secondary/Tertiary: 311 (61.22%)
Sedentary life	224 (44%)
	<b>Mean (SD)</b>
Age (years)	61.41 ± 3.87
Weight (kg)	79 ± 17.34
BMI(kg/m <sup>2</sup> )	28.29 ± 5.18

BMI: Body mass index

**Table 3.** Differences between baseline visit (V1) and final visit (V5)

	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	p
Total cholesterol (mg/dl)	216.28	204.4	203.03	198.59	196.42	< 0.001
HDL-C (mg/dl)	46.98	48.04	48.50	49.10	49.58	< 0.001
LDL -C (mg/dl)	136.40	126.99	125.03	121.02	118.97	< 0.001
Triglycerides(mg/dl)	158.37	147.06	143.88	139.45	142.17	< 0.001
Blood glucose (mg/dl)	100.73	101.88	101.34	98.92	99.29	ns
BMI (kg/m <sup>2</sup> )	28.92	22.74	28.62	28.43	28.40	< 0.001
SBP (mm Hg)	132.38	129.22	129.34	129.17	127.54	< 0.001
DBP (mm Hg)	81.30	80.32	80.01	79.13	77.63	< 0.001
WC (cm) Women	92.71	92.01	92.0	91.82	90.58	< 0.001
Men	103.1	101.70	102.60	101.23	100.76	< 0.001

p = V1 vs. V5. HDL-C: High density lipoprotein-cholesterol. LDL-C: Low density lipoprotein-cholesterol. SBP: Systolic blood pressure. DBP: Diastolic blood pressure. BMI: Body mass index. WC: Waist circumference.

activity, weight loss and a healthy diet provide specific benefit is constantly increasing. However, the major limitation to this non-pharmacological approach is the little or inconstant adherence to such strategies in the general population. (22)

This little adherence is conditioned by the patient and the time needed to prepare meals or the cost of healthy food. Other causes include the lack of time for physical activity and other well-known factors related to the patient or to the socioeconomic environment, especially in middle- and low-income countries as ours.

However, physicians are also responsible for this as they have not been adequately prepared for an effective communication with the patient. In this sense, the ENASE study was developed as a program to train physicians in the knowledge of good dietary habits and exercise to help patients to incorporate

healthy behaviors in everyday life.

The investigators attended motivational training meetings and completed self-evaluation tests. Training consisted on education in nutrition concepts, implementation of eating programs and weight loss, and, particularly, strategies focused on communicating with patients. Also, the investigators participated actively in sessions explaining how to perform physical exercise.

It should be noted that apart from training, the investigators received printed information material for patient's support, a DVD containing routine of physical training and permanent technical assistance support throughout the whole study.

These instruments allowed physicians to encourage their patients to incorporate lifestyle changes in 17 provinces and in the Autonomous City of Buenos Aires.

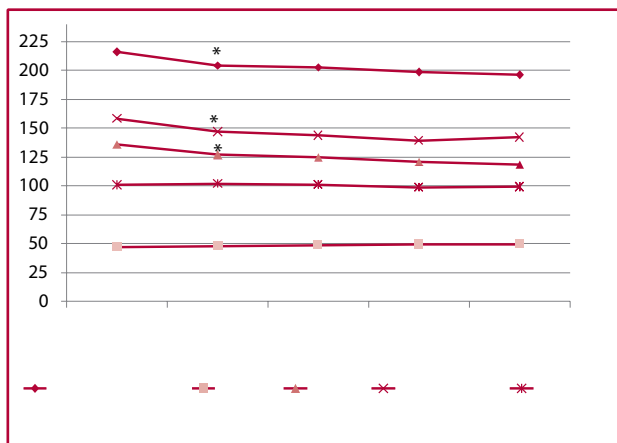


Fig. 1. Changes in risk factors from visit 1 to visit 5.

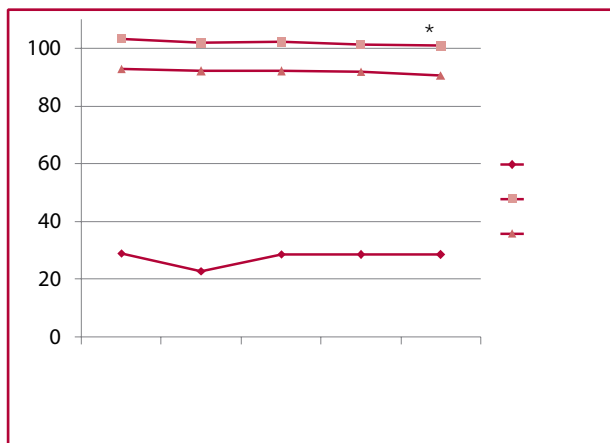
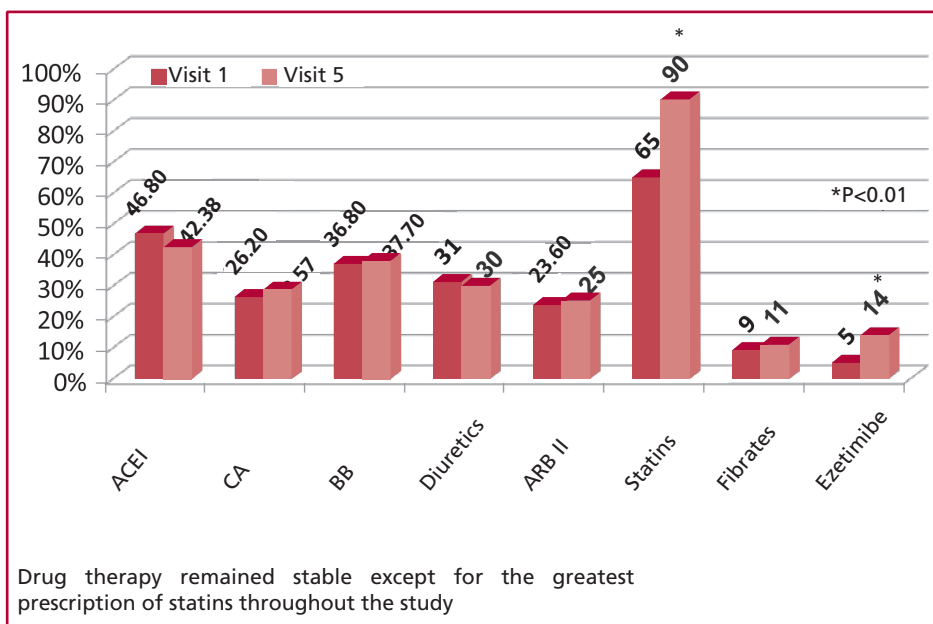


Fig. 2. Changes in risk factors from visit 1 to visit 5.

Fig. 3. Use of antihypertensive and lipid lowering agents from visit 1 to visit 5





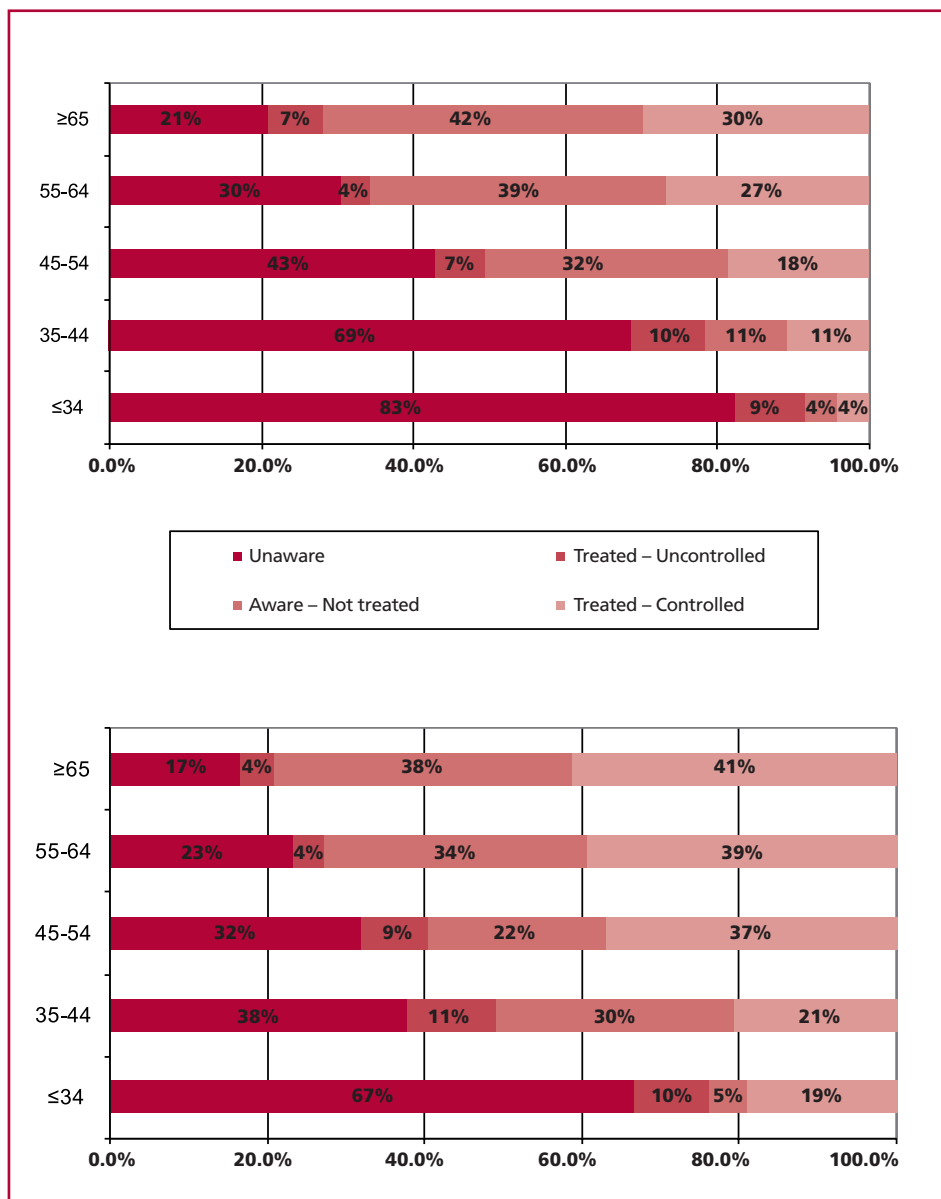


Fig. 4. Awareness, treatment and control of hypertension by gender and age Men.

This study demonstrates the feasibility of improving the clinical outcomes of a broad spectrum of patients with a high incidence of risk factors by emphasizing education and encouraging patients to adopt lifestyle changes.

The fact that these benefits became evident 6 months after the study was initiated highlights the favorable changes in the early stages of the intervention in these patients.

Although we did not find a significant reduction in body weight, we observed improvement in the metabolic parameters, suggesting changes in body composition (reduction in fat mass with increased muscle mass).

There was a slight, yet significant increase in the use of statins (65 patients at baseline vs.90 patients in the final visit) due to the expanding indications

of these agents (20, 23). However, the final effect on plasma lipid levels cannot be attributed only to the pharmacological effect, as there was also a significant reduction in lipids in subjects who were not taking statins.

There were no changes in the other medications during the study.

Smoking habits showed a 4% reduction in our population, a percentage that is higher compared to the one reported for the brief intervention (medical counseling) that is 1 to 3 %.

**CONCLUSIONS**

The ENASE study demonstrates the feasibility of training physicians in strategies to achieve lifestyle changes in their patients. Educating educators may provide mid- and long-term benefits with low costs.

**RESUMEN****Resultados de un estudio multicéntrico, no controlado, de seguimiento sobre factores de riesgo cardiovascular****Introducción**

La enfermedad cardiovascular sigue siendo una de las principales causas de muerte en nuestro país y está bien documentado que cambios adecuados en el estilo de vida son favorables tanto en términos de prevención primaria como secundaria. Sin embargo, en el mundo real, estas medidas no son de fácil instrumentación o mantenimiento. Esto llevó al desarrollo del estudio ENASE, que se concibió como un programa de entrenamiento del médico en el conocimiento de buenos hábitos de alimentación y ejercicio y en cómo ayudar al paciente a que pueda incorporarlos en forma metódica en la vida cotidiana.

**Objetivo**

Evaluar si un plan de educación del médico asistencial puede producir cambios en los pacientes.

**Material y métodos**

Estudio prospectivo, no controlado, multicéntrico, con seguimiento a 3 años en 17 provincias y en la Ciudad Autónoma de Buenos Aires, que incluyó 508 pacientes. Para el análisis estadístico se emplearon la prueba de la t de Student para muestras apareadas y la prueba de Wilcoxon.

**Resultados**

Con la guía del médico de cabecera, esta población en estudio incrementó la actividad física y realizó cambios significativos en la alimentación. A partir del primer año y con progreso adicional hasta los 3 años, se observó una reducción significativa de la presión arterial, los triglicéridos, el colesterol LDL y de la glucemia respecto de los datos basales. El colesterol HDL se incrementó en forma significativa, en tanto que el peso sólo mostró un leve descenso, no significativo.

No hubo cambios en la prescripción de fármacos durante los 3 años, con excepción de un incremento en el uso de estatinas, acorde al mayor espectro de indicaciones sugeridas por las normativas nacionales.

**Conclusiones**

Este estudio demuestra que un plan de educación y entrenamiento del médico para actuar en el paciente produce beneficios significativos en la salud cardiovascular.

**Palabras clave** > Educación - Prevención - Factores de riesgo cardiovascular - Ejercicio - Nutrición

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**ENASE work committee**

Dr Judith M. Zilberman, Dr Luis Cicco, Eliana Woronko, Dr Nora Vainstein and Dr Alberto Villamil

**ENASE study investigators**

Altamirano J., Anauch D., Baigorria M., Basile M., Barbaggio R., Cagnolo C., Casas G., Contreras F., De Cerchio A., De Giovanni E., Deketele F., Eibar S., Eljatib A., Falco S., Ferre Pecora F., Fusaro S., Galetto S., Ghigi Sager R., Echegoyen C., García Garcés J., Grippo S., Hermida M., Hernández C., Hernández J., Imsteyf E., Irusta J., Kairuz P., Moguillansky R., Morini S., Olivetto J., Paez O., Patocchi C., Pereyra S., Ponce J., Puertas E., Riselli R., Saieg M., Sambadaro G., San Damaso J., Sanz G., Scasso G., Suárez J., Ucedo E., Beltrame, Zacarias J.